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MEDICAL NEWS LETTER

Editor - Captain L. B. Marshall, MC, USN (RET)

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Policy

The U. S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be nor susceptible to use by any officer as a substitute for any item or article in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

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Notice

Due to the critical shortage of medical officers, the Chief, Bureau of Medicine and Surgery, has recommended, and the Chief of Naval Personnel has concurred, that Reserve medical officers now on active duty who desire to submit requests for extension of their active duty for a period of three months or more will be given favorable consideration.

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Residency Training in the Navy

Applications for residency training are requested from Regular officers and those Reserve officers who have completed their obligated service under the Universal Military Training and Service Act, as amended. Reserve officers with obligated service may become eligible for training upon transfer to the Regular Navy.

Training is available for Regular officers in all of the major medical specialties. It is available for Reserve officers in Pathology, Orthopedic Surgery, Obstetrics and Gynecology, Pediatrics, Urology, Anesthesiology, Otolaryngology, Dermatology and Syphilology, Ophthalmology, and Internal Medicine.

Members of the current intern class who are eligible and have been accepted for training may start their residency immediately on completion of their internship. It is now the desire of the Bureau of Medicine and Surgery to continue a resident in training without interruption until he has completed the formal training requirements leading to certification by an American Specialty Board. This procedure will be strictly adhered to in every case where the demands of the service permit, and providing the officer shows satisfactory progress. (ProfDiv, BuMed)

Effects of High-Yield Nuclear Explosions

Considerable information on the effects of the explosions of atomic weapons has been made public by the Government since the first nuclear detonations in 1945. The handbook, "The Effects of Atomic Weapons," published in 1950, is being revised and brought up to date to include the effects of thermonuclear weapons, as a result of the most recent tests at the Pacific Proving Grounds.

The effects of nuclear tests are evaluated for civil defense planning as well as for military and technological purposes. So long as nuclear weapons are in possession of any unfriendly power, the Atomic Energy Commission believes the American public will wish to be as fully informed as possible as to the nature and extent of the dangers of nuclear attack and of the protective measures that can be taken by individuals and communities to avoid or minimize those dangers if we should be attacked.

Test conditions, which must necessarily form the principal basis of evaluating the effects of nuclear explosions, may differ markedly from those which might be expected if nuclear weapons were used against our population in wartime. It would be difficult to predict the size or kind of bomb an enemy might use against us in event of war, the exact means of its delivery, the height at which it would be exploded, or the number of bombs which might reach a given target.

A nuclear detonation produces four major characteristics--blast, heat, immediate nuclear radiation, and residual radioactivity. Of these, the first three are essentially instantaneous, while the fourth has a more protracted effect. The phenomena of blast, heat, and nuclear radiation from the detonation of a thermonuclear bomb are of the same nature as those of earlier and smaller atomic bombs. The nature of the phenomena is, in general terms, standardized whether the bomb be a 20,000-ton (TNT equivalent) atomic weapon or a thermonuclear one of many times that power. The intensity and area of the blast, heat, and nuclear radiation increase in relation to the greater energy yield of the explosion.

Residual radioactivity, although in no sense exclusive to high yield thermonuclear detonations, does become a matter of major concern when a large thermonuclear device of the type used in the 1954 tests in the Pacific is exploded. The fallout of radioactivity from such an explosion, may, under certain conditions, settle over wide areas.

The effects of blast and heat from a nuclear explosion are relatively localized. One A-bomb of the earliest type equivalent to 20,000 tons of TNT (20 kilotons) would produce blast sufficient to destroy or damage severely residences within a radius of more than one mile from the point of burst. Within a radius of about a mile and a half, residences would be so damaged as to be unusable without repairs. A principal hazard to human beings would come from flying and falling debris and from fires

due to such causes as broken gas and electric lines or overturned stoves. The area in which injuries to human beings would be caused by blast, therefore, would be about the same as the area of damage to structures.

The United States, as announced previously, has developed fission bombs many times as powerful as the first A-bombs, and hydrogen weapons in the ranges of millions of tons (megatons) of TNT equivalent. For these larger weapons, the blast effects can be calculated approximately by means of a scaling law, namely, the distance at which a given blast intensity is produced varies as the cube roots of the yields of the explosions.

Similarly, the heat and burn effects of nuclear explosions can be estimated from accumulated data. These effects, of course, are influenced by prevailing atmospheric conditions. The time element also is a prime factor. Very large weapons deliver heat over an appreciably greater period of time than smaller weapons. A given quantity of heat from a high-yield weapon, delivered over a longer period of time, will produce somewhat less severe burns than the same quantity of heat from a nominal detonation.

The hazard from both burn and blast effects in the outer affected areas would be reduced greatly by shelter. Clothing or almost any kind of shelter would reduce the danger of direct burns, although there might be danger of clothing and structures becoming ignited. Also, shelter would materially reduce the hazard of blast injury by affording protection against flying or falling debris. The Federal Civil Defense Administration has made extensive studies of shelters and has issued plans for several simple and inexpensive types which can be utilized by householders. As is generally known, the shelter afforded by ordinary city buildings would not suffice within the central area surrounding the point of burst of a large nuclear weapon. For this reason, the Federal Civil Defense Administration recommends evacuation of the central areas of target zones on early warning of approaching attack.

The immediate nuclear radiation, i.e., the neutrons and gamma rays released instantaneously with the explosion of a large weapon on or near the ground, does not present a serious hazard beyond the area where heat and blast are of great concern.

Particles with residual radioactivity produced by a detonation (as opposed to the immediate nuclear radiation) may fall out over an area much larger than that affected by blast and heat, and over a longer period of time. All nuclear detonations produce radioactive materials, but the nature and extent of the radioactive fallout depends on the conditions under which the bomb is fired. The main radioactivity of a bomb's fallout decreases very rapidly with time--for the most part, within the first hours after the detonation. In an in-the-air explosion where the fireball does not touch the earth's surface, the radioactivity produced in the bomb

condenses only on solid particles from the bomb casing itself and the dust which happens to be in the air. In the absence of material drawn up from the surface, these substances will condense with the vapors from the bomb and air dust to form only the smallest particles. These minute substances may settle to the surface over a very wide area--probably spreading around the world--over a period of days, or even months. But they descend extremely slowly with the result that, by the time they have reached the earth's surface, the major part of their radioactivity has been dissipated harmlessly in the atmosphere, and the residual contamination is widely dispersed.

If, however, the weapon is detonated on the surface or close enough so that the fireball touches the surface, then large amounts of material will be drawn up into the bomb cloud. Many of the particles thus formed are heavy enough to descend rapidly while still intensely radioactive. The result is a comparatively localized area of extreme radioactive contamination and a much larger area of some hazard. Instead of wafting down slowly over a vast area, the larger and heavier particles fall rapidly before there has been an opportunity for them to decay harmlessly in the atmosphere and before the winds have had an opportunity to scatter them.

The area of hazard from radioactive fallout from a surface or near-surface explosion of a thermonuclear weapon is much larger than the areas seriously affected by heat and blast. The large radioactive cloud of a thermonuclear explosion rises with great rapidity to the highest levels of the atmosphere and spreads over hundreds of square miles in the first hours. During this time the winds toss the extremely radioactive particles about and the pattern of the radioactive fallout is determined by the size of the particles and by the direction and velocities of the winds, including those up to 80,000 feet and above. The nature of the surface of the earth on which the bomb is fired also must be taken into consideration. Because of these variables, it is impossible to apply a single fallout pattern to all thermonuclear detonations, even test explosions conducted under selected conditions. However, with adequate knowledge of atmospheric conditions, including wind directions and velocities up to high levels and meteorological reports, the fallout region for any detonation usually can be predicted with considerable accuracy. In general terms, the region of severe fallout contamination from the detonation of a thermonuclear weapon fired on or near the surface can be described as an elongated, cigar-shaped area extending down-wind from the point of burst.

The roentgen is the commonly accepted unit of measurement of radiation dosage. A dose of about 25 roentgens of radioactivity received by a person over a brief space of time will produce temporary changes in the blood. A dose of some 100 roentgens received in a short interval may produce nausea and other symptoms of radiation sickness. About 450 roentgens delivered over a day or so might be fatal to approximately half of the

persons so exposed. However, because of the body's repair processes, a total radiation dose which would be serious if incurred in a few minutes would produce much less effect if spread over a period of years.

A test explosion, at ground surface, contaminated a cigar-shaped area extending approximately 220 statute miles down-wind and varying in width up to 40 miles. In addition, there was a contaminated area up-wind and cross-wind extending possibly 20 miles from the point of detonation. Data was collected from 25 points on 5 atolls located from 10 to 330 miles down-wind (generally east) from Bikini Atoll. The estimated contour of the pattern of fallout is, therefore, based only in part on data obtained from actual measurements and partly on extrapolation, i. e., calculations based on known data, including factual information obtained during previous tests of smaller devices.

Data from this test permits estimates of casualties which would have been suffered within this contaminated area if it had been populated. These estimates assume: (1) that the people in the area would ignore even the most elementary precautions; (2) that they would not take shelter but would remain out of doors completely exposed for about 36 hours; and (3) that in consequence they would receive the maximum exposure. Therefore, it will be recognized that the estimates which follow are what might be termed extreme estimates because they assume the worst possible conditions.

On the basis of data from this and other tests, it is estimated that there was sufficient radioactivity in a down-wind belt about 140 miles in length and of varying width up to 20 miles to have seriously threatened the lives of nearly all persons in the area who did not take protective measures. Inside Bikini Atoll at a point 10 miles down-wind from the explosion it is estimated that the radiation dosage was about 5000 roentgens for the first 36-hour period after the fallout. The highest radiation measurement outside of Bikini Atoll indicated a dosage of 2300 roentgens for the same period. This was in the northwestern part of the Rongelap Atoll, about 100 miles from the point of detonation. Additional measurements in Rongelap Atoll indicated dosages for the first 36-hour period of 2000 roentgens at 110 miles, 1000 roentgens at 125 miles, and, farther south, only 150 roentgens at 115 miles from Bikini.

Some distance farther from the point of detonation, at about 160 miles down-wind and along the axis of the ellipse, the amount of radioactivity would have seriously threatened the lives of about one-half of the persons in the area who failed to take protective measures. It is estimated that the radiation dosage at that point was about 500 roentgens for the first 36-hour period.

Near the outer edge of the cigar-shaped area, or approximately 190 miles down-wind, it is estimated that the level of radioactivity would have been sufficient to have seriously threatened the lives of 5 to 10% of any

persons who might have remained exposed out of doors for the first 36 hours. In this area the radiation dosage is estimated at about 300 roentgens for the first 36-hour period.

About 7000 square miles of territory down-wind from the point of burst was so contaminated that survival might have depended upon prompt evacuation of the area or upon taking shelter and other protective measures. At a distance of 220 miles or more down-wind, it is unlikely that any deaths would have occurred from radioactivity even if persons there had remained exposed up to 48 hours and had taken no safety measures. The estimates cited above do not apply uniformly throughout the contaminated area inasmuch as the intensity of radioactivity within a region of heavy fallout will vary from point to point due to such factors as air currents, rain, snow, and other atmospheric conditions. Because of this and because most persons, if given sufficient warning probably would evacuate the area or take shelter and other precautionary measures, the actual percentage of deaths could reasonably be presumed to be considerably smaller than these extreme estimates. (U.S. Atomic Energy Commission)

(This article will be concluded in the Medical News Letter of April 15, 1955)

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Clinical Use of Potassium Para-Aminosalicylate (KPAS)

Para-aminosalicylic acid (PAS), in conjunction with streptomycin or isoniazid, is of proved value in the treatment of tuberculosis. Many patients are unable to derive the full benefit of PAS, however, because of commonly associated side effects, chiefly anorexia, nausea, vomiting, and diarrhea. The sodium salt and other preparations of PAS have been utilized in efforts to overcome these untoward reactions, generally with only limited success.

Accordingly, the present study was undertaken to determine the usefulness and "patient-acceptance" of this new preparation, namely, potassium para-aminosalicylate (KPAS). The present report summarizes experience with the clinical use of KPAS from November 1953 to August 1954.

A total of 64 patients with tuberculosis have received KPAS therapy to date. Included were 60 subjects with pulmonary tuberculosis, one with tuberculous cervical adenitis, 2 with tuberculosis of the hip, and one with Pott's disease.

Ninety-five percent, or 61 of the 64 patients treated, were found to tolerate KPAS in 12 gm. daily doses without difficulty. This finding appears even more remarkable when it is considered that 38 patients, comprising 59% of the entire group, had been intolerant to prior therapy with PAS or

NaPAS. Surprisingly enough, the admittedly disagreeable taste of the solution was not a problem, possibly because each patient was told of it prior to institution of therapy. Patients appeared to become accustomed to the taste rapidly, and many expressed preference for the liquid form of medication rather than the usual tablets or capsules.

The importance of constant refrigeration and protection from light of solutions of KPAS cannot be overstressed. Some patients who had taken full doses of KPAS for months without difficulty did develop gastrointestinal symptoms when given stale or unrefrigerated solutions.

Aside from the obvious practical importance of general patient acceptance, there are certain additional advantages of the potassium salt over the sodium salt of PAS. One of these is in the treatment of patients who also have cardiac impairment or frank congestive heart failure. Pulmonary tuberculosis is becoming an increasing problem in older men who frequently have concomitant cardiovascular-renal diseases and for whom the administration of large amounts of sodium is contraindicated.

Another potential advantage of KPAS lies in the relationship between potassium and nitrogen storage. The work of Cannon, Frazier, and Hughes showed that animals fed supplementary potassium in addition to a basal ration grew at a greater rate, had better appetites, and consumed greater amounts of food than did the control animals.

The question of possible potassium toxicity from the use of KPAS may be raised. There was no evidence of its occurrence in these patients, nor has it been noted in the more extensive experience with potassium para-aminobenzoate (KPAB).

It should be noted that patients in the present study did not receive KPAS as the sole therapeutic agent. The drug was used along with either streptomycin or isoniazid, or both. No attempt was made to redetermine the efficacy of the various drug combinations or to compare the effects of PAS and KPAS with respect to the disease process. The scope of the present study was confined to an evaluation of the patient acceptance and tolerance of KPAS.

No final statement concerning the optimal dosage of KPAS can be made at this time. Further studies of plasma PAS concentrations using different dosage schedules, comparisons with other salts of PAS, and studies of PAS concentrations in pleural and cerebrospinal fluids are being carried out. From these observations, it is concluded that the administration of KPAS, in the manner detailed in this article, offers a superior means of PAS therapy which carries a high degree of patient tolerance and acceptance. (Molthan, L., Cohen, R. V., and Zarafonetis, C. J. D., Clinical Use of Potassium Para-Aminosalicylate, KPAS: Am. Rev. Tuberc., 71: 220-227, Feb., 1955)

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Management of Chronic Nephritis

By careful and continuous supervision, the internist can accomplish much for the patient with chronic nephritis. Although cure, which would of necessity involve the replacement of damaged or destroyed functional units of the kidney, is impossible, the patient may be helped to lead a productive and comfortable life. He may be tided over the period of sudden worsening of his renal insufficiency caused by an acute infection. He may be saved from fatal potassium intoxication secondary to an injury or operation attended by disturbance in water balance. Finally, he may be made more comfortable by measures designed to control acidosis, nausea, dehydration, and other symptoms seen in the advanced stages of chronic nephritis.

In certain patients with chronic glomerulonephritis of fairly long duration and with severe renal insufficiency, the lesion seems to be, at least partially, reversible. In the absence of specific therapy, improved function would raise the question as to whether there may not be an occasional patient in whom restitution of functional units or "healing" may take place even though the process would appear by usual criteria to be chronic. Although there is no way of recognizing this group beforehand, their maintenance through a period of severe renal insufficiency is certainly most rewarding.

When the physician considers the problem of chronic nephritis, he generally thinks of the later stages of the specific renal disease glomerulonephritis, which at its inception at least, was associated with a type-specific hemolytic Streptococcus. Actually, the presenting clinical manifestations in the later stages of renal disease are somewhat similar, whether the original disorder was glomerulonephritis, pyelonephritis, or polycystic disease of the kidney. Similarly, in certain cases of hypertensive vasculorenal disease, the picture is that of renal insufficiency indistinguishable clinically, and distinguished with great difficulty pathologically, from the later stages of glomerulonephritis.

In addition to the foregoing conditions, the later stages of somewhat more unusual renal disorders may present many problems in management that have features in common with the management of glomerulonephritis. In these conditions, the renal lesion is usually one manifestation of a multisystem disease. These disorders include amyloid disease involving the kidney, lymphoblastoma of the kidney, lupus erythematosus, periarteritis nodosa, chronic vitamin D intoxication, overfunctioning of the parathyroids, the milk-alkali syndrome, sarcoidosis, and obstruction of the lower part of the urinary tract with back-pressure atrophy of renal substance. Although the nephrotic syndrome, with its picture of edema, albuminuria, hypoproteinemia, and hypercholesterolemia, is frequently seen as a stage in glomerulonephritis and, more rarely, in other chronic

renal disorders, its management is not discussed in this article.

Occasionally, persons with chronic nephritis attended by a mild degree of renal insufficiency, as indicated by the various tests mentioned, feel quite well, carry on a normal program of activity, and may be completely unaware that they are afflicted with any disease. The symptoms of chronic nephritis are interesting in that, when they develop, they are generally not those of the nephritis directly but some bodily derangement, more or less correctable, secondary to functional failure of the kidney.

Weakness or exertional dyspnea related to anemia may be the symptom that causes the patient to seek advice from his physician. Sometimes the initial and presenting symptom is anorexia or nausea. It is not unusual for the patient to recount the story of polyuria, increased fluid intake, and what he terms a "bad taste" in the mouth. Although occurring only when there is severe renal insufficiency, hiccough may be a very troublesome symptom.

Another group of symptoms consists of those related to arterial hypertension. Headache is one of the commoner of these. It is at times severe and occasionally intractable. Another symptom, related to hypertension and the associated vascular disease, is sudden and severe reduction in visual acuity. Occasionally, this visual loss provides the impetus which leads the patient to seek medical attention. Somewhat rarer is the sudden onset of diplopia due to the fact that a tiny vascular lesion of the brain stem has involved a nucleus of the cranial nerves that control eye movements. Finally, the entire symptom complex of congestive heart failure may be present in those patients who have had hypertension long enough and severely enough to cause myocardial insufficiency. In addition to the edema of congestive heart failure, evidence of fluid retention may more rarely be present, as previously mentioned, on a nephrotic basis or the basis of poorly understood hormonal or electrolyte disturbances in the terminal phase of chronic nephritis.

Symptoms of advanced renal insufficiency include hyperpnea which may be extremely distressing in the patient who has severe, uncompensated acidosis. The differentiation of this symptom from the dyspnea of congestive heart failure is important from a therapeutic standpoint. Tetany, in the authors' experience in the Mayo Clinic, has been extremely rare, although it has been seen in young adult patients. This symptom, which is related to calcium disturbance, is to be distinguished from muscular twitchings seen in the terminal stages of uremia. The exact cause of muscular twitchings, a phenomenon of increased irritability, has not been satisfactorily defined. Both the twitchings and the convulsions of terminal uremia may be the result of several separate factors. They constitute the most dramatic and, to the patient's relatives and often to the patient, the most distressing of all the symptoms of chronic nephritis. Extreme weakness and even paralysis due to hypokaliemia have been reported. A

hemorrhagic tendency, seen in some patients, may be expressed in severe bleeding or chronic oozing from the mucous membranes.

Measures which will possibly prevent the development or progression of the disorder are discussed under diet, electrolyte balance, treatment of anemia, treatment of hypertension and congestive heart failure, and treatment of uremia.

The patient who has chronic nephritis with renal insufficiency is more dependent on his physician than is the patient suffering from any of many other chronic diseases. This is due to two things. One is the multiple functions that may be deranged, namely, excretory, water-regulating, acid-base-regulating, and possibly blood-pressure-regulating functions. The second is that, with loss of the natural ability to regulate as, for instance, acid-base balance, certain measures need to be applied which will make the regulatory task easier or enhance the damaged organ's ability to perform the work. Each patient presents an individual problem and needs to be impressed with the necessity of remaining under the physician's close observation. The condition may change so that what is excellent advice at one period may be quite inappropriate at another time.

The physician has a big responsibility regarding the patient's morale. To many, a diagnosis of nephritis, because of popular conception, is the source of deep anxiety. A somewhat optimistic attitude would certainly seem justified by the increase in practical knowledge of renal function and the problems of electrolyte and water management. The patient will certainly sense the increased confidence the physician feels in directing treatment as he has available accurate data from his colleagues in the laboratory. Admittedly, a point in renal failure incompatible with life continues to exist, but if that point is set back and the course approaching that point is made smoother, then the effort expended by physician and patient has been rewarded. (Daugherty, G. W., Management of Chronic Nephritis: Arch. Int. Med., 95: 247-255, Feb., 1955)

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Liver in Congestive Heart Failure

Hepatic abnormalities constitute common and important secondary effects of congestive heart failure. Considerable information has been accumulated on the liver in heart failure, including anatomic changes, biochemical alterations, and physiologic disturbances. The present report is based on histologic studies of the liver correlated with clinical and biochemical findings in 75 patients with congestive heart failure. The investigation was undertaken to further the evaluation of the mechanism and significance of hepatic abnormalities in chronic circulatory congestion.

Seventy-one (95%) patients had hepatomegaly; 37 (49%) patients had ascites; 16 (21%) patients had jaundice; nine (12%) patients had splenomegaly;

and 8 (11%) patients had hepatic pain. The incidence of clinical abnormalities was proportionately the same in the sexes. Neither type of heart disease nor duration of heart failure could be correlated with signs and symptoms. On the other hand, the occurrence of jaundice and hepatic pain was related to the acuity and severity of failure. Each of the patients with jaundice had Grade 4 heart failure. Hepatic pain occurred in patients with acute onset of failure or an exacerbation of chronic failure.

Liver function studies revealed biochemical changes in each of the 75 patients. Serum protein alterations were uniformly present. Decreased glycogen storage was present in 93% of the patients, prothrombin deficiency in 90%, abnormal Bromsulphalein retention in 78%, and hyperbilirubinemia in 40%. A positive cephalin flocculation was present in 37% of the patients, hyperglobulinemia in 34%, cholesterol ester dissociation in 21%, elevated alkaline phosphatase in 17%, and a positive thymol turbidity in 11%. Sex, age, type of heart disease, duration of heart failure, and severity of heart failure had no consistent influence on hepatic dysfunction. Prolonged, severe heart failure was associated with the most marked degrees of biochemical changes.

Needle biopsy of the liver showed normal liver or passive congestion in 47 (63%) patients, central necrosis with congestion in 7 (9%) patients, centrilobular fibrosis with congestion in 9 (12%) patients, diffuse fibrosis in 9 (12%) patients, fatty metamorphosis in 2 (2.5%) patients, and focal inflammation in one (1.5%) patient. Histologic alterations could not be related to the type of heart disease, heart size, electrocardiographic findings, or presence of arrhythmia. The severity of heart failure and previous dietary habits were important determinants of anatomic changes. Severe heart failure was accompanied by central necrosis and exudation in the space of Desse. Recurrent episodes of failure led to centrilobular fibrosis in a patient followed over a four-year period. Fatty liver and diffuse fibrosis occurred in patients whose previous diet was grossly deficient in protein. Alcoholism was the chief cause of dietary inadequacy in these patients. Serial biopsy showed the transition of fatty liver to diffuse fibrosis in two patients.

A study of the liver in congestive heart failure improves prognostic and therapeutic perspective. Use of a composite approach including clinical, biochemical, and histologic study is desirable in patients with hepatomegaly or fluid accumulation resistant to treatment. The hepatic lesion is as important as the cardiac dysfunction in patients with diffuse fibrosis of the liver. Careful attention to replacement and supportive therapy is necessary to forestall complications of liver disease.

Serial biopsy of a large number of patients with heart failure is necessary to determine the usual mechanism responsible for diffuse fibrosis of the liver in heart failure. It has been shown that ventral fibrosis which appears to begin under the stimulus of anoxia may progress to involve

the entire liver. This study supports this thesis but demonstrates that poor nutrition with a fatty liver may also be the precursor of the diffuse fibrosis encountered in heart failure. Provision of an adequate diet and early recognition and treatment of fatty liver are essential for prophylaxis.

A problem outside the scope of this paper is concerned with the influence of liver injury on normal cardiac dynamics. Clinical study occasionally reveals the onset of heart failure with progression of hepatic insufficiency. Kowalski and Abelman have demonstrated an increased cardiac output in one-third of the patients with cirrhosis of the liver. This becomes a practical problem when one considers the possibility of concomitant hepatic and cardiac injury with nutritional deficiency.

The association of fluid retention and primary liver disease suggests that alteration of hepatic function during heart failure may contribute to chronic circulatory congestion. The excretion of antidiuretic substance in liver disease and heart failure has been extensively studied; however, its role in congestive heart failure is not completely understood. Disturbance of a common regulating mechanism which controls renal tubular activity is probably responsible for fluid retention in both liver and heart disease. Hepatic vein hypertension, hypoalbuminemia, and decreased renal blood flow may represent critical factors which provoke fluid retention. Further study is desirable to determine specific relationships of anatomic, physiologic, and biochemical changes to fluid accumulation. (White, T. J., Leevy, C. M., Brusca, A. M., and Gnassi, A. M., The Liver in Congestive Heart Failure: Am. Heart J., 49: 250-257, Feb., 1955)

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Pulmonary Edema

Recently, a well trained internist asked the Department of Radiology to show him the chest films of one of his patients in the hospital. He was startled when the films presented a massive, discrete, flocculent, butterfly pattern radiating from the hila or central zones of the lungs because no pulmonary lesion was suspected clinically. The first question the radiologist asked was the patient's nonprotein nitrogen. It was 136 mg. per 100 cc.

In the course of the consultation it was brought out that the patient was a twenty-one year old white, female stenographer with chronic glomerular nephritis. Her general health had been poor since the age of four when she had acute glomerular nephritis. She was tired and listless and suffered numerous attacks of asthma.

This incident and other similar experiences prompted the authors to make a clinical and roentgenological study of pulmonary edema with emphasis on the roentgen pattern of pulmonary edema and its differential diagnostic significance.

Acute pulmonary edema may begin with terrifying suddenness or may gradually develop from a mild form of paroxysmal nocturnal dyspnea which is frequently alleviated when the patient sits up or walks about. From this mild stage, the patient may develop cardiac asthma manifested by considerable shortness of breath (with special difficulty in the expiratory phase), orthopnea, and great anxiety.

The chronic form may be quite insidious. Some shortness of breath and cough, productive of blood-tinged sputum, are often noted in nephritics with pulmonary edema. Orthopnea is not always present. When the edema is central, rales may be inconstant or absent. In cases in which pulmonary edema is associated with nephritis, one frequently notes nausea, vomiting, anemia, petechiae, and ecchymoses in the skin, hypertension, an elevated nonprotein nitrogen, and occult or gross blood in the stools.

The pulmonary edema, stressed by the authors, is the subacute or chronic form which frequently exists with such subtle clinical manifestations that it may be easily overlooked by the attending physician. It has been noted that the roentgenogram of the chest is frequently the first indication of the presence of pulmonary edema.

This study consists of 100 cases of pulmonary edema abstracted from a total number of 982 patients considered to have entities which were known to produce episodes of pulmonary edema. These entities included clinical cases of bacterial endocarditis, hypertensive heart disease, rheumatic heart disease, syphilitic heart disease, coronary thrombosis, nephritides, and pneumonias. In addition, there were isolated interesting cases found among transfusion reactions, pheochromocytoma, carbon tetrachloride poisoning, and multiple myeloma with uremia. In this series, there were no cases due to the inhalation or aspiration of toxic pulmonary irritants. The gross proportion of pulmonary edema cases is approximately 10%. In comparing the incidence of pulmonary edema in uremic cases with that in cardiac patients without uremia, it was found that approximately 7% of the uremic patients had pulmonary edema, roentgenologically, and 12% of the cardiac group had pulmonary edema.

The 100 cases of pulmonary edema are divided into three main categories according to the morphologic features described in the foregoing classification: 90 central edema, 7 diffuse edema, and 3 focal edema.

In this series, it was striking to observe how often pulmonary edema was confused with pulmonary infarction or bronchopneumonia. Pulmonary infarction appears to be a logical diagnosis because of the signs of congestive failure, enlarged heart and hemoptysis. A point in favor of pulmonary edema is the absence of pleural pain. The two conditions--pulmonary edema and infarction--often coexist.

When the patient has a fever and leukocytosis, bronchopneumonia suggests itself. It is difficult to ascribe a high fever and signs of infection to pulmonary edema alone. Both clinical and necropsy evidence points to

the conclusion that pulmonary edema is often complicated by bronchopneumonia, or vice versa. No doubt, in a patient who is on the precarious edge of compensation, a respiratory infection or any type of infection, by putting more demand on the cardiovascular system, may tip the balance in favor of pulmonary edema.

Particularly in nephritic cases, the diagnosis of gastrointestinal malignancy is entertained. The evidence such as nausea, vomiting, weight loss, anorexia, anemia, and gastrointestinal bleeding makes an excellent case for malignancy.

The rare type of focal edema which produces a spherical mass in the lung often strikes both the clinician and radiologist as a lung tumor, either primary or metastatic. One case traveled half-way round the world for a lung operation, only to have the mass disappear on medical management.

From a roentgen viewpoint, the authors noticed frequent cases of pulmonary edema which were first diagnosed as pulmonary tuberculosis, pneumoconiosis, sarcoid, infarct, and bronchopneumonia. Conversely, in their experience, it has been rare to find a case of misdiagnosed pulmonary edema that was actually another entity. The only two cases discovered were one of sarcoid and one of tuberculosis, and there was some doubt in the latter case as to whether there was an element of edema complicating the proven tuberculous infection. (Gould, D. M., Torrance, D. J., Pulmonary Edema: Am. J. Roentgenol., 73: 366-374, March 1955)

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Phenylbutazone in Treatment of Rheumatoid Arthritis

Phenylbutazone (Butazolidin) has provided symptomatic relief of the articular phenomena of gout, rheumatoid arthritis, and rheumatoid spondylitis in a sufficient number of patients to warrant further objective appraisal of its value. Lack of influence on the sedimentation rate, coupled with initial reports of a high incidence of toxicity, has handicapped general acceptance of this drug. Thus, therapeutic evaluation of phenylbutazone would best await evidence of its objective value in the rheumatic diseases, as well as the incidence and severity of undesirable effects which might be expected to attend its use. Despite the lack of significant changes in the sedimentation rate upon administration of phenylbutazone in rheumatoid arthritis, there is evidence of a singular anti-inflammatory action of the drug when compared to other pyrazol derivative analgesics.

As with any antirheumatic drug, the following questions might be applied to phenylbutazone: (1) Is the drug truly effective and does the evaluation of its effectiveness take into consideration such matters as the natural vagaries of the rheumatic diseases, the enthusiasm of the

physician, and the concurrent use of general supportive measures? (2) Can the effectiveness of the drug be demonstrated by objective means? (3) Can an effective dose be given without producing disturbing side effects? (4) Does the drug produce toxic effects which persist after the drug has been withdrawn? (5) After initial improvement, can the remission of the arthritic process be maintained over a significant period of time; or, is the ultimate course of the disease altered?

Many observers agree that phenylbutazone is highly effective in symptomatic relief of the articular phenomena of rheumatoid arthritis, rheumatoid spondylitis, and gout. This fact is borne out by the favorable response after administration of the drug as well as by return of symptoms following its withdrawal or decrease of dose below an effective level. Placebo-controlled studies of the drug have been conducted without detracting from this opinion. Clinical course of the patients was independently evaluated by the three clinical members of the investigating team. The PR (serum protein-polysaccharide ratio) values were made known to the clinical members in the latter portion of the study as an aid in arriving at the minimal effective dose for each patient. An effort was made to limit medication to the single drug under study, and patients were questioned at each visit as to previous medication. It is realized, however, that many patients with rheumatoid arthritis have an extensive personal armamentarium from which they are prone to supplement the prescribed therapy unless under a rigidly supervised program.

As previously reported, the PR serves as a useful index of clinical activity in rheumatoid arthritis. Further evidence is presented that a similar situation exists in gout and lupus erythematosus.

In the production of significant changes in the PR, phenylbutazone compares favorably with cortisone and corticotropin in rheumatoid arthritis, rheumatoid spondylitis, gout, and perhaps lupus erythematosus.

The frequent incidence of toxic reactions to phenylbutazone, although usually mild, constitutes a considerable handicap, even to the conservative use of the drug. Thus, in 14% of the cases presented, discontinuance of the drug was considered necessary due to undesirable side reactions, an incidence in agreement with the figure of 15% reported by Kuzell and associates. A higher incidence of toxic effect (20%) has been reported by Brodie and co-workers, using higher doses of the drug (800 mg. per day). Although no clear brief can be presented as to whether phenylbutazone will become a standard agent for treatment of the rheumatoid diseases, the present evidence would indicate that it is of objective value in suppressing fundamentally harmful processes accompanying rheumatoid arthritis with a reasonable factor of safety.

No persistent toxic effects have been observed after withdrawal of the drug in the series presented. This is in agreement with the extensive study of Kuzell, although several deaths have been reported

concurrent with phenylbutazone administration. Whether the beneficial therapeutic response to phenylbutazone represents alteration of the course of the rheumatic diseases or merely suppression of symptoms must await more prolonged studies, although present data would seem to indicate the latter concept. The natural variability of the clinical course of rheumatoid arthritis compels a most conservative attitude concerning the evaluation of any therapy. It would appear, however, that any suppression of inflammatory activity should be eagerly sought from the standpoint of relief of subjective distress and to the end of minimizing crippling which might result from this inflammation.

The similarities of the phenylbutazone and cortisone effects on the PR and the dichotomy of their effect on sedimentation rate and possible mode of action are of extreme interest.

Upon evidence presented, it would appear that in many patients with rheumatic diseases, an effective dose of phenylbutazone can be prescribed with a reasonable factor of safety. It is felt that the PR has served as a valuable aid in determining the minimal effective dose of phenylbutazone and in demonstrating its objective value in the treatment of rheumatoid arthritis. (Payne, R. W., et al., The Value of Phenylbutazone in the Treatment of Rheumatoid Arthritis as Determined by Clinical Response and by the Serum Protein-Polysaccharide Ratio (PR): J. Lab. & Clin. Med., 45: 331-339, March 1955)

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Tumor Outline of Esophageal Carcinoma

The roentgen diagnosis of carcinoma of the esophagus is usually based upon the alterations seen in the barium-filled lumen, such as filling defects produced by the fungating tumor, excavations due to necrotic ulcers, obstruction, suprastenotic dilatation, perforation, and indentations by paraesophageal lymph node metastases. The extension of the tumor is usually determined from the length of the lesion as indicated by the filling defect. This is the basis for surgical indications and statistics.

This procedure is unsatisfactory because it fails to outline the tumor in its lateral extent and, therefore, does not satisfy the general principles of tumor localization for which all the dimensions of the lesion should be determined: length, width, and depth. The intramural and/or extraesophageal extension may significantly affect therapeutic indications and prognosis. Also, the added knowledge of lateral or depth extension may influence radiation technic and selection of fields.

Although direct visualization of the esophageal tumor, radiographically, should be regarded as of diagnostic and therapeutic significance, it would seem to be a neglected field. Only short sporadic notes on this subject were found in the American and English literature.

Identifying and differentiating the shadow of an esophageal tumor may, at times, be difficult. One may encounter enlarged hilar or mediastinal nodes; the margin of the scapula, clavicle, or manubrium sterni may be superimposed on the esophagus and its surrounding structures. The descending aorta or the aortic arch may also cause errors in interpretation. A careful analysis of the soft-tissue shadows in more than one view will usually exclude such mistakes. Post-irradiation interpretation may also be difficult because the paraesophageal tumor may be replaced by fibrotic tissue.

Rarely, post-tracheal tumor shadows have their origin from organs other than the esophagus. In such cases, differentiation is easily accomplished by barium filling of the esophagus.

In reviewing earlier cases, the authors found that in only a small percentage was the tumor visualized directly. Later, with improved technic and increased attention to this problem, demonstration was obtained with increasing frequency. There appeared to be no special technic which, of itself, permitted visualization of the tumor. Any good technic, resulting in high-contrast films, may satisfy the requirements. With low-voltage ranges, good films of the barium filling are obtained but the penetration is not sufficient for differentiation of the complex peri-esophageal shadows. High-voltage films are usually more satisfactory.

The most suitable views are the lateral and right anterior oblique. For detailed data relating to tumor extension, however, four views are usually required: postero-anterior, lateral, right and left oblique. In lesions of the cervical or uppermost thoracic segments of the esophagus, an additional lateral plain film of the neck is helpful, along with barium study of the hypopharyngeal structures. In those cases where contrast filling of the cervical esophagus is not possible, or where an attempt to fill the esophagus with contrast medium would produce serious discomfort, plain films are invaluable. (Haas, L. L., and Baker, B., Tumor Outline of Esophageal Carcinoma: Radiology, 64: 241-247, Feb., 1955)

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Carcinoma of the Prostate

Approximately 15% of all men over 55 years of age who come to postmortem have been shown to have definite carcinoma of the prostate which may or may not have brought about clinical manifestation of the disease. Investigations have also shown that, in the Clinic at the University of Iowa Hospitals, approximately 20 to 25% of all patients who need treatment for bladder neck obstruction have carcinoma of the prostate. Because of the high incidence of this particular neoplasm, considerations of therapy and management are of exceptional importance.

At present, the only type of curative therapy that is efficacious in an appreciable number of cases is radical surgical removal of the disease in its early stages. Because, as has been demonstrated by Young, this lesion starts in the outer part of the prostate in 95% of cases, symptoms of bladder neck obstruction, or other symptoms due to the carcinoma, do not occur early. They occur late in the disease when the tumor has progressed to the urethra, distorting it and interfering with urination, or when the tumor has metastasized and produced pain due to the location of the metastasis. Early diagnosis is essential if curative therapy is to be instituted, and this can be secured only by rectal examinations every six months after the age of 50, and adequate biopsy studies of suspicious areas.

Early diagnosis can be made only by means of routine rectal examination and study of suspicious areas which are demonstrated on rectal examination. Subacute and chronic prostatitis of any etiology, prostatic calculi, and occasionally, nodules of hypertrophy cause confusion in diagnosis. If, in the course of a routine physical examination, such a lesion is found by rectal examination in a patient who is under 70 and in good physical condition, x-ray films should be made to determine if a prostatic calculus is present. If none is found, if there is no pyuria, or if there is a little tenderness over the area which might indicate the presence of an infectious process which should clear up with appropriate therapy in the course of a week or two, then biopsy must be considered.

Biopsy of suspicious lesions may be readily obtained by one of several means. The Silverman needle perineal punch biopsy is carried out easily and has little danger except that a poor sample may be obtained which may be misleading. The perineal and retropubic technics are performed without difficulty and may then go on to radical surgery if this is indicated by study of the frozen section. The transurethral technic is satisfactory if the suspicious lesion can be brought up into the mouth of the resectoscope. The transrectal technic has proved satisfactory, although the authors believe that it carries more danger of injury to the rectum if a radical prostatectomy is performed later.

Papanicolaou's stain of prostatic secretion is ordinarily not useful for two reasons: (1) It may be misleading in that typical carcinoma cells will not be seen and the sample is much poorer than that obtained by the Silverman needle technic which is just as easy to perform; and (2) The intensive massage necessary to obtain satisfactory cells is more likely to cause dissemination of the tumor than it would be with any of the other biopsy technics. This can be demonstrated by the ease with which the serum acid phosphatase of the blood is raised by prostatic massage in known benign hypertrophy cases as well as in carcinoma cases. The serum acid phosphatase, therefore, is of little importance in itself unless the conditions, under which the blood sample is obtained, are known.

Once a definite diagnosis of carcinoma has been made, therapy must be instituted. In those persons who are in good condition, who are 70 years of age or younger, and who have a localized lesion, radical prostatectomy is the treatment of choice.

In those patients in whom the tumor has progressed beyond the confines of the prostate, invading the pelvic fascia laterally or the fascial planes about the seminal vesicles, Jewett and Young found that cure is rarely obtained. In these instances, it would seem that interstitial irradiation is indicated, with removal of as much of the tumor as possible.

If the lesion is too large for irradiation therapy or if bony metastasis is present, palliative therapy, in the form of relief of bladder neck obstruction by transurethral prostatic resection and endocrine therapy, is the only means available. Endocrine therapy brings about definite relief of pain in the majority of patients and, in some patients, apparently retards the growth of the tumor. There are sporadic cases in which the metastasis has disappeared, but usually, except for local regression in the size of the prostate and lowering of the serum acid phosphatase, the tumor does not regress for a significant period following orchiectomy, estrogen therapy, or a combination of these therapies. It is still a moot question as to just when orchiectomy or stilbestrol therapy should be administered and whether they should be given at the same time or one after the other. In late cases, with relapse of both estrogen therapy and orchiectomy, pain may be difficult to control. In some of these cases, adrenalectomy or ablation of the pituitary gland may produce a temporary remission. These procedures are still experimental. Occasionally, however, dramatic improvement can be achieved for six months or a year. X-ray therapy to painful lesions may be of great value in this stage of the disease. (Flocks, R. H., and Prendergast, L. J., Treatment of Carcinoma of the Prostate: Geriatrics, 10: 52-58, Feb., 1955)

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Radioactive Colloidal Gold in Treatment of Cancer

This article presents the experience of the authors with the use of radioactive colloidal gold in the treatment of cancer. The favorable effect of this isotope in inhibiting the formation of serous effusions caused by malignant disease has been commented upon by numerous observers. The authors' experience has been almost equally divided between the intracavitary and interstitial use of Au 198.

Intratumor injections of Au 198 are capable of delivering large amounts of ionizing radiation within a tumor without over-irradiating the surrounding normal tissues. This is possible because, first, the source of radiation is contained directly within the tumor, and second, most of

the radiation has a short range of penetration. External sources of radiation, such as roentgen ray, on the other hand, give the skin and normal tissues overlying the tumor more radiation than the tumor, in accordance with the inverse square law. The limiting factor in radiation dosage is the tolerance of the normal tissues surrounding the tumor, but the ability to place the source of radiation within the tumor automatically permits a larger dosage to be administered. The theoretical advantages of colloidal gold over other internal sources of radiation, such as radium needles or radon seeds, are due to its physical properties, particularly its short half-life, its radiation spectrum, and the fact that it is in a fluid medium. The short half-life of Au 198 permits the dosage to be delivered within a brief period of time; and there is no necessity to remove the source of radiation at a later date, as is the case with radium and other isotopes with long half-lives. The fact that the radioactivity is contained in a fluid medium which can be easily injected makes it theoretically possible to disperse many point sources of radiation throughout the tumor.

The authors based the selection of patients for treatment with radiogold on three premises. First, there should be a reasonable chance for benefit to the patient without undue hazard from the procedure. Second, the isotope should not be used in lieu of other modes of therapy which would be more beneficial to the patient. Because they rigidly adhered to the foregoing criteria, the series consists predominantly of patients in the terminal stages of malignant disease and is heavily weighted with short-term survivals. Third, the histologic diagnosis of malignant tumor should be confirmed prior to the use of the isotope.

Intratumor injection of radioactive colloidal gold 198 offers certain theoretical advantages over more conventional methods of radiation therapy. By providing a source of short-range ionizations directly within the tumor, it produces sharper localization of radiation than is possible with long-range ionizations such as roentgen ray, radium, or radon. This sharper localization makes possible the treatment of deep-seated lesions which previously were beyond the scope of radiation therapy because of the limits of tolerance of the surrounding normal tissues. Because of the decreased amount of radiation which the normal tissues receive, this form of therapy also has the advantage of not being associated with radiation sickness. A further advantage of this sharp localization is that it permits the use of higher dosage levels.

More than two years' clinical experience with intratumor injection of this isotope has led to two main conclusions. One is that Au 198 is a potent carcinolytic agent, and the other is that its usefulness is sharply limited by the biological characteristics of the individual tumor. If a tumor characteristically metastasizes early and widely, the benefit to the patient from the destruction of an isolated tumor nodule is negligible. On

the other hand, if the tumor is one which characteristically metastasizes slowly and regionally, then the ability to destroy isolated tumor nodules in locations not easily treated by roentgen ray or surgery, may afford very good palliation. Cases of intra-abdominal cancer have been discouraging because of the propensity of these tumors for disseminated spread at, or following, the time of treatment. In some of the tumors which tend to remain localized, however, it has constituted a relatively simple, safe, and locally effective form of therapy. In general, it has seemed that gold therapy is indicated and is even promising in cases where there is a localized tumor nodule which cannot be effectively treated by conventional methods, and which is not accompanied by disseminated disease. This therapy also appeared to be useful in the destruction of isolated tumor nodules which were accompanied by widespread metastases whenever these nodules either caused the patient great physical pain or psychological distress. The procedure can be carried out simply, safely, and with little or no discomfort or inconvenience to the patient.

The only toxic side reaction noted in this study was the occurrence of hypoplasia of the bone marrow in four patients who received a dose of more than 50 millicuries. Total body radiation undoubtedly played some role in this phenomenon, but the authors believe that a major factor was the presence of particles of gold in the marrow itself. These appeared to represent gold which had found its way into the blood stream following intraperitoneal injection, or else had been injected directly into the blood stream during intratumor injections of very vascular tumors. Apart from this potential hazard to the hematopoietic system, the material was found to be quite free of any toxicity detectable clinically or by routine laboratory tests.

The authors are in complete accord with others, that the intracavitary application of Au 198 is of value in the treatment of serous effusions due to carcinoma. Their experience with pleural effusions with this therapy has been excellent.

The present policy, adopted in the treatment of cancer with Au 198, is as follows: First, it is believed that this is the treatment of choice for patients with peritoneal or pleural effusions caused by malignant disease. Second, the interstitial application of Au 198 is reserved for those patients with malignant tumors that tend to spread via the lymphatics or are locally invasive. Lesions that are rapidly and widely disseminated by the blood stream are not suitable for this form of therapy. Third, this radioactive isotope should not be used in place of roentgen ray therapy except in instances where the latter has proved to be ineffective or cannot be applied for other reasons. Fourth, all patients who receive more than 50 millicuries of Au 198 should have a complete blood count every week for three months because of the possibility of damage to the bone marrow. (Wheeler, H. B., Jaques, W. E., and Botsford, T. W., Experiences with the Use of Radioactive Colloidal Gold in the Treatment of Cancer: Ann. Surg., 141: 208-217, Feb., 1955)

Who Should Take the Biopsy?

This article opens with the emphatic statement that whether an individual has the title of M. D., D. M. D., or D. D. S., has little to do with his qualifications to take a biopsy in the mouth, to perform more extensive surgical operations about the jaws, or to read a microscopic slide.

With the publicity given cancer by the American Cancer Society and others, and with the increase in cancer education and training in medical and dental schools sponsored by the U. S. Public Health Service, there has been a great increase in interest and attention paid to all phases of the diagnosis and treatment of malignant disease, including the biopsy procedure. All dental students are now taught that any lesion which does not heal in approximately three weeks should be clinically regarded as malignant disease and that a biopsy should be taken to establish or refute that diagnosis.

Another often quoted dictum is that the one who first sees a patient with cancer of the oral cavity holds the life of that patient in his hands, and if he, dentist or physician, considers the possibility of cancer and secures a biopsy, the patient's prognosis is thereby appreciably improved.

The question as to who should take the biopsy when such lesions are discovered, and as to how it should be taken, is very important. The author has observed what he considered grave mistakes in the examination of cancer patients. Vigorous palpation is often employed by the surgeon, by his assistants, and by students attending the clinic to elicit characteristic signs of induration and fixation, both locally and in the drainage lymph node areas. Then a local anesthetic solution may be injected into the suspected area, followed by incisions extending into the peripheral tissue, and on occasion, into the underlying periosteal tissue. Then the area is closed with sutures. The author is strongly of the opinion that such methods as he has described of obtaining a biopsy specimen of these lesions of the oral mucosa are not conducive to improving the rate of cures which, excluding cancer of the lip, is approximately 50%.

The physician's point of view is always conditioned by his past experience and associations. For some years the writer was closely associated with the Department of Pathology at the Harvard Medical School and the Children's Hospital in Boston. Dr. Sidney Farber at the Children's Hospital, in dealing with abdominal tumors of children, recognized years ago the danger of indiscriminate palpation of such masses. An inflexible rule in that hospital is that no palpation of an undiagnosed abdominal mass in a child may be done, except by the physician or surgeon in charge of the patient. The author has been further influenced by discussions with the group working on the cancer problem at the University of Pennsylvania. The surgeons, headed by Dr. I. S. Ravdin, recently have become much concerned, on clinical grounds, with the liabilities of the biopsy procedure.

Dr. Baldwin Lucké commented that modern statistical methods should be applied to the evaluation of the effects of the biopsy, using tumors with a high tendency to metastasize under a variety of experimental conditions.

Carcinomas of the oral mucous membrane have a high metastasizing potential and a high degree of killing power. Allen and Spitz state, "the melanocarcinomas may probably be considered of a virulence equal to, or greater, than Grade IV, epidermoid carcinomas." Perhaps it is justifiable to invert this statement and say that the more undifferentiated squamous-cell carcinomas of the oral region have a virulence approximating that of melanocarcinomas.

Many warnings have been issued against biopsy of a pigmented lesion of the oral mucosa which may prove to be melanocarcinoma. The author believes that physicians should consider carefully the way in which they biopsy, or advise biopsy, of clinically early lesions which may prove to be the much more common, but little less dangerous, epidermoid carcinomas of the oral cavity.

The author finds it difficult to believe that a surgeon or pathologist, oral or general, familiar with the course of malignant disease originating in the oral cavity, would permit unnecessary palpation of a possibly malignant lesion in his own mouth, or injection of an anesthetic solution into the immediate vicinity of such a lesion; or, finally, that he would permit anyone to incise into the affected area, except the oncologist who assumes responsibility for treatment of the lesion when the diagnosis has been established, and who should take due cognizance of the potential danger of incising a tumor of high metastasizing power.

Most dentists ordinarily do not make professional decisions where the life of the patient is at stake. Oral surgeons and oral pathologists are notable exceptions to this rule. In far-advanced cancer of the oral cavity, the question of who is to take the biopsy, or how it is to be taken, becomes of little more than academic interest. In early, small lesions, where proper diagnosis and adequate treatment are imperative, the method of obtaining the biopsy specimen may be all-important if eventual cure is to result.

A great many practicing dentists do not even extract teeth. To expect such dentists to perform a biopsy properly, particularly of a small lesion, is not reasonable. A dentist who sees his patient regularly at stated intervals, often over many years, may and does function well as a finder of lesions, not only of the oral mucosa but of the lips, face, hands, and other areas. In addition, he should be informed of the possible significance of hoarseness, persistent cough, loss of weight, and other danger signals. He is being trained in all dental schools at present to examine thoroughly the soft tissues of the mouth and oropharynx.

When the biopsy is taken, the operator should be aware of the potential dangers to the patient. Prompt treatment is of great importance.

Palpation, massage, and incision have been shown to favor early and widespread metastases of highly malignant tumors in experimental animals. The less differentiated squamous-cell carcinomas of the oral cavity have a virulence (tendency to metastatize and to kill the patient) which is of the same order as that of melanocarcinomas (malignant melanomas).

Malignant neoplasms have a stage during which they invade locally but do not metastasize spontaneously. This stage is relatively long in most cancers of the lip and, to a lesser extent, of the hard palate and gingiva of the upper jaw. Cancers originating in other parts of the oral mucous membrane tend to spread via the lymphatics and less often by blood vessels while the lesions are clinically small. Microscopically, the bulk of the lesion, like an iceberg, extends beneath the surface laterally and in depth. Both the local growth and metastatic growths proliferate for a time before they can be detected by clinical examination.

In the past five years about one case per 100, submitted to the Laboratory of Oral Pathology of the University of Pennsylvania for microscopic examination, has revealed a neoplastic growth which was not suspected clinically. Cancers, like bacterial infections, appear to be held in check temporarily by the surrounding normal tissues. Periosteum, in particular, may resist penetration by cancer cells for a period unless surgically disturbed. Surgical incision may destroy the natural barriers and the granulation tissue of repair favors rapid growth of the neoplasm.

Cancer, though relatively uncommon, is the most serious disease which the dentist is likely to encounter. The diagnosis is made by evaluation of all data, clinical, roentgenologic (if involving hard structures), and microscopic. In most instances, the taking of a biopsy when the clinical impression is squamous-cell carcinoma should be performed by a specialist who by training and experience is best qualified to do so, and who will assume responsibility for the treatment. (Boyle, P. E., Who Should Take the Biopsy? Oral Surg., 8: 118-122, Feb., 1955)

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Change of Address

Please forward requests for change of address for the News Letter to: Commanding Officer, U. S. Naval Medical School, National Naval Medical Center, Bethesda 14 Md., giving full name, rank, corps, and old and new addresses.

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The printing of this publication has been approved by the Director of the Bureau of the Budget, June 23, 1952.

Rotation Sequence and Tours of Duty

The normal rotation sequence for Medical Department officers is sea-shore-foreign shore-shore. Duty tour lengths are influenced by several factors. These include, but are not limited to, the ratio of afloat and foreign shore billets to those ashore, number of officers on active duty for limited specified periods, requirements for specialist qualifications, billets of an unusually arduous nature or in isolated locations, and training requirements. The tour lengths indicated below are considered to be normal, for Reserve and Regular medical officers, but in individual cases the influences mentioned above may require deviations from them.

a. Normal tour lengths afloat are two years.
b. Normal tour lengths on foreign shore are promulgated by Naval Personnel Instruction 1300.15A.
c. Normal tour lengths with Fleet Marine Force are:
   (1) 1st MarDiv 24 months
   (2) 2nd MarDiv 24 months
   (3) 3rd MarDiv 12-15 months in Japan
d. Normal tour lengths of duty ashore in the continental United States are three years for officers in the rank of lieutenant commander through captain; all others two years. (PersDiv, BuMed)

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Board Certifications

American Board of Internal Medicine

LT Newton W. Allebach (MC) USNR (Active)
LT Richard Foulk (MC) USN
LT Paul L. Richburg (MC) USNR (Active)

American Board of Neurological Surgery

LT Robert W. Rand (MC) USNR (Active)

American Board of Orthopedic Surgery

CDR Warner D. Bundens, Jr. (MC) USN
LCDR George W. Hyatt (MC) USN

American Board of Radiology

LT John A. Fleming (MC) USNR (Active)

American Board of Surgery

CDR Marvin L. Gerber (MC) USN
LT Henry P. Royster (MC) USNR (Active)
CAPT Derrick C. Turnipseed (MC) USN
CDR David J. Williams Jr. (MC) USN

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From the Note Book

1. Rear Admiral W. P. Dana, MC USN, Assistant Chief for Aviation and Operational Medicine and Assistant Chief for Research and Medical Military Specialties, Bureau of Medicine and Surgery; Captain E. V. Jobe, MC USN, Head, Training Branch, Professional Division; CDR F. B. Voris, MC USN, Head, Special Activities Branch, Aviation Medicine Division; and CDR R. L Christy, Jr., MC USN, Head, Aviation Medicine Liaison Branch, will represent the Bureau at a meeting to be held at the Naval School of Aviation Medicine, Pensacola, Fla., April 12-13, 1955. They will meet with representatives of the Naval School of Aviation Medicine, the American Medical Association's Council on Medical Education, and the American Board of Preventive Medicine, to inspect the School's curriculum and standards to determine its eligibility for certification as a teaching institution in aviation medicine. (TIO, BuMed)

2. Captain T. Ferwerda, MC USN, Deputy Director, Research Division, and Head of the Medical Military Specialties Branch of that Division, attended a physiological-psychological symposium held, March 10-11, 1955, at the Naval School of Aviation Medicine, Pensacola, Fla.

Sponsored by the Office of Naval Research, the meeting was attended by scientists from some fifteen states representing as many universities and such research activities as the Bell Telephone Laboratories, the Rockefeller Institute for Medical Research, and the Central Institute for the Deaf. Information concerning their research in sensory and perceptual processes was exchanged. Participants were given an over-all look at what is being done in this field, and the opportunity to determine the place of their research in the Navy program in relation to what others are doing and the problems to be solved. (TIO, BuMed)

3. Dr. H. T. Karsner, Research Advisor to the Surgeon General of the Navy, attended a meeting of the Senior Scientists of East Coast Naval Laboratories, held at the U. S. Navy Underwater Sound Reference Laboratory, Orlando, Fla., March 3-4, 1955. Dr. Karsner was the only medical representative in the group.

Among the matters discussed at the meeting were the study of underwater sound; the policies in regard to coordination of research and development in the Navy; the relations of the various bureaus of the Navy Department and the laboratories; and a proposed instruction concerning the duties and responsibilities of the technical directors of Naval laboratories. (TIO, BuMed)

4. Pensacola, Fla., -- Capt. J.C. Early, MC USN, Commanding Officer of the U.S. Naval School of Aviation Medicine, spoke at the Annual Student Symposium of the Aeronautical University, Chicago, Ill., March 2.

The subject was "Testing Techniques of Airplanes and Men." Captain Early presented the Navy method utilized in determining the limitations of the pilot and crew in high speed flight. Being both a veteran naval flight surgeon and a naval aviator, Captain Early was particularly well qualified to contribute to this aeronautical meeting. (TIO, School of Aviation Med)

5. Capt. J.V. Westerman, DC USN, Head, Personnel Branch, Dental Division, Bureau of Medicine and Surgery, attended a meeting held by the Council of Federal Dental Service of the American Dental Association, March 6, 1955, at the ADA Headquarters, Chicago, Ill. Representatives of the Department of Defense were invited to attend this meeting for the purpose of discussing the extension of special provisions of the Universal Military Training and Service Act. (TIO, BuMed)

6. The Bureau of Medicine and Surgery, Navy Department, has scheduled a conference of Medical Department finance and administrative officers to be held at the National Naval Medical Center, Bethesda, Md., April 20, 21, and 22, 1955.

The program will be presented under the direction of the Comptroller Division of the Bureau, with the active support of the Materiel Division in the supply and logistic area. The agenda will be designed to cover all phases of Naval Medical Department fiscal, accounting, supply, and related matters. (TIO, BuMed)

7. CDR A.G. Nielsen, DC USN, and CDR L.S. Hansen, DC USN, Naval Dental School, presented essays on ultrasonic cutting to the International Association of Dental Research, Morrison Hotel, Chicago, Ill., March 18, 1955. Under the general title, "Limited Animal Study of the Comparative Biologic Response to Rotary and Ultrasonic Vibration Cutting," CDR Nielsen presented certain technical approaches to ultrasonic and rotary cutting on the teeth of laboratory animals, while CDR Hansen presented the biological response of dental tissues to the two cutting methods. (TIO, BuMed)

8. Three Bureau of Medicine and Surgery scientific exhibits were shown in March 1955: "Treponemal Immobilization Studies" was displayed during the District of Columbia Venereal Disease Control Conference. The "U.S. Navy Dental Corps Casualty Treatment Training Program" was shown at the Oregon State Dental Association Meeting in Portland, and at the Washington State Dental Association Meeting in Seattle. "Aviation Medicine and the Naval Aviator" was shown during the Twenty-Sixth Annual Meeting of the Aero Medical Association held at the Hotel Statler, Washington, D.C., March 21-23, 1955. (TIO, BuMed)

9. A new type of electrocardiographic electrode has been developed at the U.S. Naval School of Aviation Medicine, Naval Air Station, Pensacola, Fla. The new electrode consists of solidified plaster of paris, containing table salt, and obviates the use of electrode pastes. The new technique saves considerable time and permits recording of the heart in rapid sequence from innumerable points on the chest immediately adjacent to each other, and from the standard positions on the limbs. A few drops of water placed initially on the new electrode is all the preparation necessary to obtain as many individual recordings as desired.

Capt. A. Graybiel, MC USN, and Lieut. L.R. Krasno, MC USN, who developed the new plaster electrocardiographic electrode, report that the recordings obtained with the new type of electrode are equally as good as those obtained with electrode pastes. They have found the new technique of special value where many patients are to be tested and when extensive electrocardiographic exploration of the chest is desired. (TIO, BuMed)

10. Announcement of a system for "x-ray televising" the internal parts of an operating engine, the demonstration of a radiation monitor for atomic blasts, and recent developments in the science of measurement were among the highlights of an open house held at the National Bureau of Standards during the week of February 7. The program--attended by several hundred leaders in the fields of science, industry, government, and education--stressed the significance of physical measurement standards to scientific and industrial progress, and featured the first showing of two new radiation facilities: the NBS Betatron, and Gamma Ray Laboratories. (National Bureau of Standards)

11. The treatment of poisoning by chlorinated insecticides involves prompt removal of unabsorbed pesticide from the stomach or from the skin, and control of convulsions by adequate sedation (intravenous barbiturates). Recovery from poisoning has been prompt and has not been followed by any characteristic sequelae. No validated "chronic poisoning" type of illness has been recognized. (Indust., Med., March 1955; L.C. McGee, M.D.)

12. In a study of refractory edema due to congestive heart failure, restoration of responsiveness to mercurial diuretics was accomplished by the production of a hyperchloremic acidosis. (Ann. Int. Med., Feb., 1955; A. L. Rubin, H. G. Thompson Jr., W. S. Braveman, and E. H. Luckey)

13. Comments received on questionnaires sent to radiologists and non-radiologists indicate a wide difference of opinion on the possible effects of relatively small but frequent doses of ionizing radiation on the offspring of exposed fathers. The data given in the article presents a picture of first generation effects. (Am. J. Roentgenol., March 1955; S. H. Macht, M. D., and P. S. Lawrence, D. Sc.)

14. An operative technique for vaginal hysterectomy is presented in detail with the use of illustrations to clarify certain steps. (Am. J. Obst. & Gynec., Feb., 1955; Capt. L. T. Dorgan, MC USN, Capt. J. J. Carter, MC USA)

15. When termination of pregnancy is indicated because of toxemia, the intravenous use of Pitocin for the induction of labor is valuable because it may effect delivery in spite of an uneffaced and undilated cervix in a patient not at term. (Am. J. Obst. & Gynec., March 1955; C. H. Mauzy, M. D.)

16. The clinical management of the anuric patient is discussed in Am. J. Med., Feb., 1955; Capt. H. C. Oard, MC USN, Cdr. G. I. Walker, Jr. MC USN.

17. A brief review of antituberculosis vaccines with emphasis on BCG is presented in J. Pediat., March 1955; J. B. Seagle, M. D.

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BUMED INSTRUCTION 11013.1 2 March 1955

From: Chief, Bureau of Medicine and Surgery
To: All Management Control Activities of the Bureau of Medicine and Surgery

Subj: Specific Work Requests; instructions for

Ref: (a) BuMedInst 11014.1 (NOTAL)
(b) BuMedInst 4860.1 (NOTAL)

Encl: (1) Specific Work Request
(2) Local Request for Estimate
(3) BuMed Check-off List
(4) Format for SWRs Requiring Approval of SecNav and SecDef

This Instruction provides instructions for obtaining approval and funds for maintenance beyond the capacity of local maintenance forces, minor new construction, alterations, and improvements to plant property. BuMed Instruction 4700.1B is cancelled.

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BUMED INSTRUCTION 5600.2B 10 March 1955

From: Chief, Bureau of Medicine and Surgery
To: Ships and Stations Having Medical/Dental Personnel Regularly Assigned

Subj: Professional articles; approval for publication and/or incurring expenses in connection with

Ref: (a) U S. Navy Regulations, 1948, Art. 1252, para. 1, 2, and 3
(b) Manual of the Medical Department, Article 1-19 (2), (3)
(c) NavOp Five of 25 Nov 1953
(d) U S. Navy Public Information Manual, Art. 0514, para. 3(d)

This Instruction is issued to outline the requirements of the Bureau with respect to approval for publication of professional articles, and with respect to the obligation of funds in connection with publication. BuMed Instruction 5600.2A is canceled.

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BUMED INSTRUCTION 7010 14 March 1955

From: Chief, Bureau of Medicine and Surgery
To: All BuMed Managed Activities

Subj: Allotments; command responsibility for administrative control of

Ref: (a) NavCompt Manual, Volume 3, Paragraphs 032000 to 032005

This Instruction reaffirms the administrative responsibilities of commanding officers and others who are administrators of allotments at activities under the management control of the Bureau of Medicine and Surgery.

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BUMED INSTRUCTION 6460. 3A 15 March 1955

From: Chief, Bureau of Medicine and Surgery
To: Stations Having Medical Personnel Regularly Assigned

Subj: Tissue homografts; follow-up studies concerning

Purpose. To promulgate instructions concerning follow-up studies in patients who have received tissue homografts in naval medical facilities.

BuMed Instruction 6460. 3, addressed to naval hospitals, is canceled.

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PREVENTIVE MEDICINE SECTION

Venereal Disease Control

New Change in T. P. I. Laboratories

The Treponemal Immobilization (T. P. I.) Test Laboratory, located with the Hawaiian Medical Laboratory at Tripler Army Hospital, Hawaii, will discontinue the performance of the T. P. I. test on 15 March 1955. After that date the Sixth Army Medical Laboratory, Fort Baker, California, will perform the T. P. I. test for the Pacific Fleet; Naval Forces in the Far East, Philippines, Marianas, Territory of Hawaii, Alaska and the States of

California, Oregon, and Washington. The T. P. I. Laboratory, Naval Medical School, National Naval Medical Center, Bethesda 14, Maryland, will serve all other areas. When specimens are submitted, care should be taken to consider the criteria for the use of this special test which will be found in BuMedInst 6222.5B. All specimens should be forwarded with NavMed Form 1351, Request for Treponemal Immobilization Test for Syphilis. These forms are now available upon requisition from appropriate district publications and printing offices.

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Navy Regulations Concerning Venereal Disease

The proper handling of venereal disease cases in the Navy can be quite perplexing to the new medical officer. As a physician he will be skilled in the diagnosis and treatment; however, as a medical officer he also has the responsibility of compliance with the various regulations of the military.

The need for regulations is often not appreciated by the uninitiated. Accustomed to thinking of the cure of his patient, the physician sometimes fails to realize the public health, moral, and social implications of venereal disease, and it is toward these aspects that regulations are directed. Some Navy regulations parallel local and state laws and the regulations of local, state, or national public health agencies. These provide for the repression of prostitution, the reporting of contacts, and the protection of the public from the infected individual. Other Navy regulations ensure uniformity in the handling of venereal diseases in order that the interests of both the individual and the Government may be protected, not only during the service of the individual but also after he becomes a veteran. Still other regulations are concerned with the responsibility of all elements of the Navy in the promotion of vigorous programs for venereal disease prevention.

The information necessary to carry out this military duty, with respect to venereal disease, will be found in the following bibliography which will serve as a quick reference guide to aid the busy medical officer:

a.	The Reporting of All Cases of Urethritis	BuMedInst 6222.1
b.	Prophylaxis Measures	BuMedInst 6222.2A BuMedInst 6222.3A
c.	Precautions in Greenland	BuMedInst 6222.4

d. The Treponema Immobilization Test for Syphilis (to describe the T. P. I. test and to set forth the criteria and procedures for its use)	BuMedInst 6222. 5(B)
e. The Training and Utilization of Venereal Disease Contact Interviewers	BuMedInst 6222. 6
f. Venereal Disease Contact Interviewing and Reporting	BuMedInst 6222. 7 NavMed P-5036
g. The Procedure for the Telegraphic Reporting of Contacts of Early Syphilis Patients	BuMedInst 6222. 8
h. The Restriction of Liberty, Transfer of Persons with Venereal Disease, Detection Concealed Cases, and Reporting of Symptoms	BuPers Manual 1953 Par. C-7818
i. Physical Standards for Enlistment of Personnel with a Venereal Disease	BuPersInst 1130. 3 Army Regs 40-115
j. Repression of Prostitution	General Order #18
k. The 8-point Agreement on Measures for the Control of Venereal Disease, Nov. 1948	NavMed P-5036 p. 9
l. The Establishment and Composition of Armed Forces Disciplinary Control Boards	SecNavInst 1620. 2
m. The Responsibility for and Action to be Taken Concerning Venereal Disease Control	SecNavInst 6222. 1
n. Some Suggestions for Treatment	Medical News Letter: Vol. 23, No. 3, Feb., 5, 1954 Vol. 23, No. 5, Mar., 5, 1954

o. From the Manual of the Medical Department:

Educational Measures	Article 3-10
Cooperation with Other Agencies	Article 3-12
Venereal Diseases	Article 14-13
The Genito-Urinary System and Venereal Disease	Article 15-22
Submarine Personnel (j) Venereal Disease	Article 15-29
Women (g) Any Venereal Infection	Article 15-34
Annual Physical Examination of Officers (j) Blood Count and Serologic Test for Syphilis	Article 15-45
Discharge, Transfer to Fleet Reserve, or Retirement of Enlisted Personnel (5) Venereal Disease	Article 15-48
Examination and Standards for Class 1, Service Group I (3) Syphilis	Article 15-62
Venereal Disease Entries	Article 16-55
Venereal Disease Control	Article 22-18
Report of Venereal Disease in Recruits (FSA-15)	Article 23-133
Separation	Article 23-134
Telegraphic Report of Contacts of Early Syphilis Cases to State Health Officers (FSA-16-1)	Article 23-135
Venereal Disease Epidemiologic Report (FSA-16)	Article 23-136

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Tuberculosis Control

Use and Technique of the Tuberculin Test

The tuberculin reaction is an acute local inflammation resulting from the injection or application of tuberculin, and is considered to be one of the most specific tests in clinical medicine. It is a safe, reliable test and a relatively simple procedure. It may give the clinician valuable information, yet not infrequently it is inadvertently omitted from the diagnostic work-up of patients. In epidemiological studies, it is of the utmost value as an index of the extent of infection in communities. It is extremely useful, not only in locating sources of infection, but also in examining contacts or as a guide in case finding. Since July 1947, under the tuberculosis control program for the U.S. Navy, all Navy and Marine Corps recruits are given tuberculin skin tests. Those found to have positive reactions are further scrutinized, and re-examined to discover possible sources of infection. The importance of the tuberculin test increases constantly as the rate of infection in the population decreases. A few years ago, when the large majority of people in this country were tuberculin positive, the chief value of the test was exclusive. Today the converse is true, and a positive test is considered a more positive indication of infection. Finally, in BCG vaccination programs, the tuberculin test has become of special significance as an indication of the "take" of the vaccine. Obviously, once BCG has been administered, the tuberculin test loses its specific value as an indicator of natural infection. This is one of the principal objections to such a program.

Special Risks. In August 1951, because of the greater exposure to tuberculosis and the higher incidence of the disease among hospital corpsmen, it was deemed advisable that tuberculin tests be made on all medical and dental personnel under the age of thirty-five first reporting to a naval hospital for staff duty, and also on those over age thirty-five if they so desire. For example, during fiscal year 1953, tuberculin tests were made on 3624 previously untested individuals serving on staffs of naval hospitals. The "single test" containing 0.0001 milligramsof purified protein derivative tuberculin, was used in most instances. Of the 3624 individuals tested, 2647, or 73%, were found to be negative. This high rate of negative reactors emphasizes the large reservoir of susceptible persons who are apt to have intimate contact with the infectious cases.

Those whose tests are "negative" or "doubtful" are retested at annual intervals while on duty in the hospital as long as the reactions remain "negative" or "doubtful". Appropriate physical and laboratory examinations are made of personnel whose tests convert to positive and arrangements are made for more frequent chest x-rays and continued medical observation for at least 2 years. In 1953, for example, 4567 of those medical department

personnel who had given negative reactions within the year were retested with the "single test" dose. In this group it was found that 392, or 8.5% had converted to a positive tuberculin reaction. If it is considered that the so-called "doubtful reactions" may be a latent manifestation of tuberculin sensitivity, then another 61 must be added to this group of "converters" resulting in a total of 9.9%. This percentage is considerably lower than that found in many studies of hospital personnel throughout the nation. In the latter studies, conversion rates were noted to be as high as 39.2%.

Even though the conversion rate in the Navy seems to be comparatively low, it is considered advisable to continue the search for unknown cases of tuberculosis. Vigilance can be facilitated by the routine chest examination of every hospital admission by the photofluorographic method where the incidence of tuberculosis is found to be four times that of the general population, and also by the continued periodic retesting of those negative reactors who, by virtue of their duties, are caring for potentially actively tuberculous patients.

Because the tuberculin test indicates that the individual has been infected by the tubercle bacillus, by inference, tuberculous lesions are present in the individual, but in the large majority of cases these are too small to be roentgenographically demonstrable. The vast majority of these primary infections heal, and the only clinical evidence of their presence is a tuberculin reaction; later their sites may be revealed roentgenographically by the appearance of densities of calcification in the tracheobronchial lymph nodes or in the lung parenchyma. Experience has shown that, of all those who react to tuberculin, it is possible to demonstrate a pulmonary or lymph node focus roentgenographically in less than 25%, and symptoms of a primary infection in adults are frequently absent. In most of those who acquire a primary infection of tuberculosis, the lesions heal and clinical pulmonary tuberculosis never develops. If the primary infection does not heal properly, clinical tuberculosis usually is evident within a 2-year period.

In contradistinction to the usually benign course of primary infection in adults, during the first few years of life this frequently progresses to tuberculous meningitis with an extremely high mortality rate. Because of this, a program is currently being undertaken at 19 pediatric centers throughout the United States under the coordination of the tuberculosis control program of the Public Health Service in order to study the effectiveness of chemotherapy in preventing serious complications and death in this age group. All children under 2 years of age with primary tuberculosis, as evidenced by conversion to a positive tuberculin test, and children between 2 and 12 years of age who convert to a positive tuberculin reaction and show x-ray evidence of primary infection will be placed on a prophylactic course of isoniazid for one year.

A reaction to certain specified amounts of tuberculin is an indication of tuberculous infection. With few exceptions, definite sensitivity to tuberculin, once acquired, persists through life. This sensitivity may vary in

intensity and may temporarily decrease or disappear in the course of high fever, exanthematous disease, miliary tuberculosis, and the last stages of pulmonary tuberculosis. A very small percentage of persons (less than 5%) may fail to react to tuberculin even after infection resulting from exposure to cases of open tuberculosis or after the administration of vaccine prepared from living or dead tubercle bacilli. The tuberculin test remains negative in a high percentage of cases of sarcoidosis.

At the present time, Purified Protein Derivative (PPD) and Old Tuberculin (OT) are widely used. Purified Protein Derivative is the tuberculin of choice, and is recommended as the standard for comparative studies. It is carried on the Navy Stock Catalog under five categories which include varying numbers of tests per unit at three different strengths. PPD is prepared by growing tubercle bacilli on a synthetic medium of known composition. The tuberculin protein produced in the medium is then obtained by precipitation with ammonium sulfate at neutrality and by further purification.

The method of choice in administering tuberculin and the one recommended for accuracy and for all general purposes is the intracutaneous (Mantoux) test. This is described as the standard procedure and will be described in the following paragraphs. The scarification (Pirquet) test, and the Vollmer patch test are not considered as accurate, and will not be described here because they are not recommended for general use.

Intracutaneous or Mantoux Test. The intracutaneous tuberculin test is best carried out by injecting the desired concentration of PPD or Old Tuberculin into the cleansed volar skin of the forearm. This injection is made with a short (half-inch) sharply beveled 24 or 25-gauge platinum or steel needle and a tuberculin syringe. For satisfactory results, dry sterilized tuberculin syringes which have been tested previously for leakage and are not used for the administration of other materials except tuberculin, should be used. Care must be exercised by the operator to insure that the exact determined amount of solution is injected, and that it is injected intracutaneously and not subcutaneously. When the injection is properly made, a wheal should appear immediately at the site of injection.

The use of a single dose of 0.0001 mg. of Purified Protein Derivative or five tuberculin units (5 t.u.), is recommended for case-finding programs. This standard single test has been used routinely for case-finding in the U.S. Navy since January 1948 This dose is recommended because persons showing roentgenographically demonstrable lesions characteristic of tuberculosis are, in the vast majority of instances, highly sensitive to PPD or Old Tuberculin. In the Navy Catalog, #6505-299-8171 contains sufficient PPD and diluent for ten tests of 0.0001 mg. (5 t.u.) each, #6505-153-8290 contains fifty tests of similar strength and #6505-153-8291 contains 250 similar tests.

A dose of 0.00002 mg. of Purified Protein Derivative or one tuberculin unit (1 t.u.) is recommended for the initial dose for those living

in areas having a high morbidity or mortality from tuberculosis, for those with a history of severe reactions following previous administration of tuberculin, for those with a history of intimate contact with persons with clinically manifest tuberculosis, and for persons with extrapulmonary forms of this disease. This dosage is generally used for diagnostic work-up of patients. No. 6505-153-8366 in the Navy Stock Catalog contains ten tests of 0.00002 mg. (1 t.u.) each.

For the present, with certain exceptions as noted, the use of a single intermediate dose (5 t.u.) is recommended. Further studies on the specificity of the larger doses of both PPD and Old Tuberculin are being made. No. 6505-153-8367 in the Navy Stock Catalog contains ten tests of 0.005 mg. (250 t.u.) each, and should be reserved for special diagnostic studies when the first strength (1 t.u.) and intermediate strength (5 t.u.) doses give a negative or doubtful reaction.

When PPD is used, the dosage should be carefully checked in order to prevent any untoward reactions. To prepare the dose of PPD required for case-finding, the tablet should be dissolved in the requisite amount of the diluent supplied so that each 0.1 ml. of the dilution will contain 0.0001 mg. PPD. When not in use, diluted solutions should be kept in a refrigerator. Solutions more than a few days old should not be used.

The intracutaneous tuberculin test (Mantoux) with either PPD or Old Tuberculin should be read 48 or 72 hours after the injection. Readings should be made in good light with the arm slightly flexed. Response to injection is classified as positive, negative, or doubtful. Reactions may be classified arbitrarily as one, two, three, or four plus, depending upon the extent of induration measured at its widest diameter. A reaction showing some definite induration more than 5 mm. and not exceeding 10 mm. in diameter is recorded as a one plus ($+$) reaction. A two plus ($++$) reaction is an area of induration measuring 10 to 20 mm. in diameter. A three plus ($+++$) reaction is characterized by marked redness and induration exceeding 20 mm. in diameter. A four plus ($++++$) reaction consists of severe induration and an area of necrosis. A reaction with a trace of induration measuring 5 mm. or less in diameter is rated as doubtful. Redness without associated induration does not constitute a reaction.

Syringes which have been used for the administration of PPD or Old Tuberculin should not be used for the administration of preparations such as coccidiodin, histoplasmin, or other diagnostic reagents, because PPD and Old Tuberculin are difficult to remove from the syringes. (Excerpted in part from Diagnostic Standards and Classification of Tuberculosis, 1950 Edition, National Tuberculosis Association)

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General Sanitation

Get the Right Thermometer

Administrative inspections of ServPac units have revealed that chemical thermometers requisitioned for use in checking temperature of fresh milk at time of receipt and for checking temperatures of dish wash and rinse waters are not suitable for the intended use.

Of the thermometers available through the General Stores Keeper, the following are recommended as being best suited for the purposes indicated:

Checking milk temperatures: Spirit Filled Thermometer, Complete, Pocket Type
30° to 120° F.
Stock No., 18-T-1359
Cost: $1.05

Checking dishwashing and water temperatures: Thermometer, Chemical
0° to 240° F., by two-degree graduation.
Stock No., 18-T-1725
Cost: $1.10

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